Supplementary Appendix

Supplement to: Bar-On YM, Goldberg Y, Mandel M, et al. Protection against Covid-19 by BNT162b2 booster across age groups. N Engl J Med. DOI: 10.1056/NEJMoa2115926

This appendix has been provided by the authors to give readers additional information about the work.

Supplementary Appendix

Contents

Data Sharing

Aggregated data and code for reproducing the results are available from the corresponding author upon request.

Supplementary Methods 1 - Database

The Ministry of Health (MOH) in Israel collects all COVID-19 related variables in a central database. These include data on all PCR tests and results, vaccination dates and type (almost all received the Pfizer-BioNTech vaccine), daily clinical status of all COVID-19 hospitalized patients, and COVID-19 related deaths. Specifically, the data used for conducting this study included vaccination dates (second and third doses), PCR tests (dates and results), hospital admission dates (if relevant), clinical severity status (severe illness or death), and demographic variables such as age, sex, and demographic group (General Jewish, Arab, ultra-Orthodox Jewish). Severe disease is defined as a resting respiratory rate >30 breaths per minute, oxygen saturation on room air <94%, or ratio of PaO2 to FiO2 <300. Those who died from COVID-19 during the follow-up period were also counted as severe disease cases in our analysis. The fact that Israel has a central health care system increases the coverage and reliability of the data. A small fraction of the population with missing observations on gender or demographic sector were excluded from our analysis. They comprised ≈0.1% of the total population and were most likely missing those variables at random. We also excluded from the analysis individuals for whom the area of residence was unknown, which amounts to about 2.5% of the total population in the database. As we show in Supplementary Analysis 2, this exclusion has a negligible effect on the results of the analysis.

The MOH database comprises data from multiple sources. These include all MOH-approved laboratories performing PCR testing in Israel, including private laboratories, hospitals and the four Health Maintenance Organizations (HMOs) that together insure the entire Israeli population. Quality assurance of data was performed extensively over the course of the pandemic, and the data are monitored daily by the MOH, and are continuously used for public health decision-making.

PCR testing for SARS-CoV-2 is free-of-charge and widely available in Israel. Testing is required for symptomatic persons (e.g., with fever or acute respiratory illness), people who were in close contact with an infected individual, or travelers returning from abroad. When undergoing a test, persons are required to provide their unique identification number. A nasal or nasopharyngeal swab is collected and sent to a certified laboratory where it is tested (using national testing standards) by reverse transcription quantitative PCR. All sampling laboratories digitally report the data to the MOH database. Turn-around intervals between nasopharyngeal sampling and test result are 48 hours at most and typically within 24 hours.

Surveillance of COVID-19-associated hospitalizations is continuously performed by the MOH. Data from all hospitals are updated daily, and often twice a day. In accordance with national guidelines, health-care providers report all hospitalizations and deaths among individuals with laboratory-confirmed SARS-CoV-2 infection.

Supplementary Methods 2 - Calculation of Adjusted Rate Differences

The adjusted rate difference was calculated separately for each age category as follows. After fitting the Poisson model, the expected number of cases in each age category was calculated twice, first assuming all individuals received the booster dose and then assuming no individual received the booster dose. These estimates were calculated by applying the results of the Poisson model to each person with and without the coefficient of the booster group in the calculation of the linear predictor: $exp(\beta_{booster} + \beta \times covariates)$ and $exp(\beta \times covariates)$, where exp is the exponential function, $\beta_{booster}$ is the coefficient of the booster group and β is the row vector of coefficients for all other covariates. The difference between these estimates (expressed per 100,000 person days) is reported as the adjusted rate difference (adjusted to the Israeli population during the study period).

Supplementary Analysis 1 - matching approach

To validate our findings, we conducted an independent analysis which relied on matching fully vaccinated individuals who received a booster dose with similar individuals who on the same day had not yet received a booster dose (meaning that they have received only two vaccine doses at least five months ago). The approach was similar to that conducted by Dagan et.al.[9], and aimed at comparing individuals' risk rather than rates based on person-days. Briefly, each individual in the booster group was matched to an individual who was in the nonbooster group on the booster-vaccination day. Matching was performed based on the following characteristics: age group (16-29, 30-39, 40-49, 50-59, 60-69, 70-79 and 80+), gender, week of second vaccine dose and demographic group (general Jewish, Arab, ultra-Orthodox). Follow-up for both individuals ended at the time of an infection, at the end of the study, or when the nonbooster individual received a booster dose, whichever occurred first. We calculated the probability of being free of infection in each of the two groups as a function of time using the Kaplan-Meier estimator, and compared the survival probabilities of the two groups at the end of the study. For each group, we calculated the probability of an event occurring between day 12 following the booster and the end of the study, among individuals still at risk on day 12. We used the ratio between the probabilities of the two groups as an estimate for the risk ratio over the study period. We generated 95% confidence intervals around this estimate using the percentile bootstrap method with 200 repetitions.

Using this approach, we obtained the following estimates (summarized in Table S15) for the rate ratio of confirmed infection between the nonbooster and booster groups: 9.5 (95% CI, 7.8 to 11.4) for persons aged 60 or older, 9.4 (95% CI, 5.2 to 13.0) for persons aged 50-59, 8.4 (95% CI, 6.2 to 10.6) for persons aged 40-49, 7.3 (95% CI, 5.7-8.7) for persons aged 30-39, 13.3 (95% CI, 5.9 to 18.8) for persons aged 16-29. For severe illness, this approach yielded a rate ratio of 12.4 (95% CI, 4.3 to 30.4) for persons aged 60 years or above. Due to the very small number of severe cases below the age of 60, and the high censoring proportion, calculation for severe COVID-19 for people younger than the age of 60 was not possible. In addition, due to the small number of COVID-19 associated deaths, calculation for deaths was not possible.

Supplementary Analysis 2 - comparison with previous analysis methods

As mentioned above, the analysis is similar to that used in our previous study for the 60 years or older population [2]; the study protocol can be found at https://www.nejm.org/doi/suppl/10.1056/NEJMoa2114255/suppl_file/nejmoa2114255_protocol.pdf. The current analysis differs in several aspects. First, to increase the number of person-days at risk for the control group in the secondary analysis, instead of using the rate of confirmed infection and severe illness 4 to 6 days post-vaccination as the control, we use days 3 to 7 post-vaccination. (The data from

our previous paper indicated that the infection rate during days 3 and 7 post-vaccination was similar to that of days 4-6). Second, we had previously excluded days at risk during the first 12 days of the booster vaccination campaign. This was done to ensure that data for the booster and control groups covered the same calendar days. The calendar day was introduced as a covariate in the Poisson regression analysis to account for the changing risk of infection. In the current analysis, we relaxed this exclusion criterion and, instead, adjusted for changing risk of infection by including as a covariate the weekly average incidence rate in the place of residence of each person, binned into 10 quantiles. Thus, the current analysis adjusts for differences in background risk using a spatial-temporal exposure risk index, which is specific for each person's residential area and changes over time.

To assess the impact of these different modelling choices on the results of our analysis, we repeated the analysis using the exact methodology used in Bar-On et al.[2]. The results are given in Tables S1 and S2, and are similar to the results of our current analysis. As can be seen when comparing Table 3 and Table S2, the main difference between the two modelling choices is that the control group in the secondary analysis now includes many more person-days, which reduces the uncertainty range of the estimated rate ratios.

Supplementary Analysis 3 - subdivision of the 60+ age range in assessing booster effects

To examine more closely the effect of the booster dose among people aged 60 years or older, we repeated the same primary and secondary analyses reported in the Methods section of the main text, but used the following age groups instead of the "60+" age group: 60-69 years of age, 70-79 years of age, and 80 years or older. The results of this analysis are provided in Tables S13 and S14. The results indicate that age groups 60-69 and 70-79 have similar rate ratios, which are higher than that of the 80+ group.

Supplementary Tables

Table S1. Summary of the Poisson regression analysis of confirmed infections using the exact original methodology of Bar-On et al. [2]

Age	Nonbooster group infections (person-days at risk)	Booster group (days 12+) infections (person-days at risk)	Early post-booster (days 4-6) group infections (person-days at risk)	Rate ratio nonbooster relative to booster days 12+ [95% CI]	Rate ratio booster days 4-6 relative to booster days 12+ [95% CI]
60+	8,101 (12,313,286)	2,834 (53,443,850)	1,130 (2,538,825)	13.1 [12.5, 13.7]	8.5 [7.9, 9.1]
50-59	5,832 (8,582,524)	1,013 (17,522,442)	470 (899,613)	13.1 [12.3, 14.1]	9.3 [8.3, 10.4]
40-49	9,853 (11,482,869)	1,159 (14,826,279)	528 (1,018,185)	12.3 [11.6, 13.1]	6.9 [6.2, 7.7]
30-39	12,965 (13,845,767)	843 (9,934,041)	534 (1,021,927)	12.3 [11.5, 13.2]	6.5 [5.8, 7.3]
16-29	10,757 (17,842,500)	317 (9,830,263)	385 (1,156,629)	20.7 [18.5, 23.2]	10.9 [9.4, 12.7]

Table S2- Summary of the Poisson regression analysis of severe COVID-19 cases using the exact original methodology of Bar-On et al. [2]

Age	Nonbooster group infections (person-days at risk)	Booster group (days 12+) infections (person-days at risk)	Early post-booster (days 4-6) group infections (person-days at risk)	Rate ratio nonbooster relative to booster days 12+ [95% CI]	Rate ratio booster days 4-6 relative to booster days 12+ [95% CI]
60+	593 (11,622,846)	166 (46,763,420)	58 (2,468,483)	19.4 [16.1, 23.3]	6.8 [5, 9.1]
40-59	95 (18,196,759)	8 (26,488,757)	1 (1,658,291)	23.8 [11.5, 49.2]	1.9 [0.2, 15.6]

Table S3: Demographic and clinical characteristics of the comparative groups including all model covariates. The table presents the proportion of person-days at risk instead of the proportion of individuals. Values are presented for the study period - July 30, 2021, to October 10, 2021.

	Nonbooster group Person-days at risk = 98,112,120				*Booster group (days 12+) Person-days at risk = 104,202,554*				*Early post-booster group (days 3-7) Person-days at risk = 16,978,846*			
Group	*% person days at risk*	*# positive infections*	*# severe COVID-19*	*# COVID-19 deaths*	*% person days at risk*	*# positive infections*	*# severe COVID-19*	*# COVID-19 deaths*	*% person days at risk*	*# positive infections*	*# severe COVID-19*	*# COVID-19 deaths*
Female	*52.0%*	*47,212*	*488*	*111*	*50.8%*	*2,995*	*68*	*12*	*51.2%*	*4,271*	*51*	*15*
Male	*48.0%*	*36,269*	*683*	*187*	*49.2%*	*3,165*	*107*	*23*	*48.8%*	*4,609*	*85*	*31*
Age 16-29	*27.2%*	*22,441*	*10*	*0*	*9.3%*	*317*	*0*	*0*	*18.4%*	*1,611*	*0*	*0*
Age 30-39	*19.7%*	*21,452*	*16*	*1*	*9.2%*	*842*	*1*	*0*	*14.5%*	*1,493*	*0*	*0*
Age 40-49	*16.9%*	*16,885*	*49*	*2*	*13.8%*	*1,157*	*3*	*0*	*16.9%*	*1,794*	*3*	*0*
Age 50-59	*13.0%*	*10,247*	*119*	*7*	*16.5%*	*1,011*	*5*	*1*	*15.8%*	*1,521*	*4*	*0*
Age 60-69	*12.0%*	*7,037*	*233*	*44*	*22.6%*	*1,265*	*32*	*5*	*15.9%*	*1,274*	*20*	*4*
Age 70-79	*7.1%*	*3,495*	*312*	*77*	*18.8%*	*915*	*46*	*9*	*12.2%*	*781*	*48*	*18*
Age 80+	*4.1%*	*1,924*	*432*	*167*	*9.8%*	*653*	*88*	*20*	*6.4%*	*406*	*61*	*24*
General Jewish	*70.8%*	*61,584*	*923*	*252*	*88.8%*	*5,180*	*154*	*31*	*86.2%*	*7,558*	*125*	*43*
Arab	*23.6%*	*14,293*	*188*	*33*	*7.1%*	*536*	*11*	*1*	*9.6%*	*617*	*7*	*2*
Ultra-Orthodox Jewish	*5.7%*	*7,604*	*60*	*13*	*4.1%*	*444*	*10*	*3*	*4.2%*	*705*	*4*	*1*
Vaccine Period Jan, 16-31	*12.7%*	*9,598*	*449*	*135*	*42.2%*	*2,487*	*102*	*27*	*29.6%*	*2,615*	*84*	*33*
Vaccine Period Feb, 1-15	*16.3%*	*13,805*	*375*	*100*	*29.0%*	*1,802*	*53*	*5*	*25.5%*	*2,414*	*36*	*11*

Vaccine Period Feb, 16-28	*14.9%*	*14,330*	*116*	*27*	*14.5%*	*1,018*	*11*	*1*	*17.8%*	*1,855*	*9*	*2*
Vaccine Period Mar, 1-15	*21.0%*	*19,148*	*112*	*22*	*10.1%*	*588*	*7*	*2*	*16.1%*	*1,341*	*4*	*0*
Vaccine Period Mar, 16-31	*26.1%*	*21,396*	*91*	*12*	*3.8%*	*243*	*2*	*0*	*8.8%*	*572*	*3*	*0*
Vaccine Period Apr, 1-15	*7.0%*	*4,456*	*23*	*2*	*0.4%*	*20*	*0*	*0*	*1.7%*	*76*	*0*	*0*
Vaccine Period Apr, 16-30	*1.6%*	*665*	*4*	*0*	*0.0%*	*2*	*0*	*0*	*0.3%*	*6*	*0*	*0*
Vaccine Period May, 1-15	*0.4%*	*83*	*1*	*0*	*0.0%*	*0*	*0*	*0*	*0.1%*	*1*	*0*	*0*
Incidence group 0%-10% decile	*7.0%*	*988*	*38*	*12*	*14.3%*	*215*	*1*	*0*	*6.9%*	*120*	*3*	*2*
Incidence group 10%-20% decile	*7.8%*	*2,343*	*55*	*15*	*13.4%*	*424*	*6*	*0*	*6.9%*	*201*	*4*	*0*
Incidence group 20%-30% decile	*10.0%*	*3,935*	*111*	*33*	*11.0%*	*487*	*13*	*1*	*6.9%*	*305*	*12*	*4*
Incidence group 30%-40% decile	*10.5%*	*5,420*	*147*	*45*	*10.2%*	*580*	*17*	*2*	*8.6%*	*522*	*16*	*8*
Incidence group 40%-50% decile	*10.4%*	*6,590*	*111*	*31*	*9.8%*	*616*	*12*	*1*	*10.1%*	*781*	*10*	*6*
Incidence group 50%-60% decile	*9.8%*	*7,682*	*104*	*22*	*9.4%*	*667*	*14*	*1*	*11.8%*	*967*	*17*	*4*
Incidence group 60%-70% decile	*10.2%*	*9,680*	*138*	*38*	*8.4%*	*626*	*26*	*5*	*13.5%*	*1,294*	*28*	*11*

Incidence group 70%-80% decile	*10.8%*	*11,647*	*136*	*31*	*8.4%*	*750*	*24*	*6*	*12.3%*	*1,335*	*20*	*6*
Incidence group 80%-90% decile	*11.1%*	*14,034*	*173*	*40*	*8.1%*	*783*	*24*	*3*	*11.7%*	*1,391*	*11*	*2*
Incidence group 90%-100% decile	*12.5%*	*21,162*	*158*	*31*	*7.1%*	*1,012*	*38*	*16*	*11.2%*	*1,964*	*15*	*3*

Table S4: Demographic and clinical characteristics of the comparative groups for people aged 60 or above. Values are presented for the study period - July 30, 2021, to October 10, 2021.

Group	Nonbooster group Person-days at risk = 22,803,132				Booster group (days 12+) Person-days at risk = 53,332,528				Early post-booster group (days 3-7) Person-days at risk = 5,844,835			
	% person days at risk	# positive infections	# severe COVID-19	# COVID-19 deaths	% person days at risk	# positive infections	# severe COVID-19	# COVID-19 deaths	% person days at risk	# positive infections	# severe COVID-19	# COVID-19 deaths
Female	57.2%	6,841	413	109	52.7%	1,300	64	12	53.4%	1,162	48	15
Male	42.8%	5,615	564	179	47.3%	1,533	102	22	46.6%	1,299	81	31
Age 60-69	51.7%	7,037	233	44	44.2%	1,265	32	5	46.1%	1,274	20	4
Age 70-79	30.5%	3,495	312	77	36.6%	915	46	9	35.3%	781	48	18
Age 80+	17.8%	1,924	432	167	19.2%	653	88	20	18.5%	406	61	24
General Jewish	81.2%	10,226	803	244	90.5%	2,481	146	30	89.5%	2,210	118	43
Arab	14.3%	1,371	126	31	5.7%	159	11	1	6.7%	105	7	2
Ultra-Orthodox Jewish	4.5%	859	48	13	3.8%	193	9	3	3.8%	146	4	1
Vaccine Period Jan, 16-31	37.5%	4,699	412	132	65.0%	1,812	100	27	60.1%	1,505	81	33
Vaccine Period Feb, 1-15	32.1%	4,030	322	95	27.5%	805	51	4	28.6%	712	35	11
Vaccine Period Feb, 16-28	9.3%	1,181	90	27	3.8%	114	8	1	4.6%	114	8	2
Vaccine Period Mar, 1-15	9.1%	1,116	71	21	2.5%	71	5	2	3.6%	88	2	0
Vaccine Period Mar, 16-31	8.8%	1,131	61	11	1.0%	26	2	0	2.4%	34	3	0
Vaccine Period Apr, 1-15	2.4%	256	17	2	0.1%	5	0	0	0.5%	7	0	0
Vaccine Period	0.5%	35	3	0	0.0%	0	0	0	0.1%	1	0	0

Apr, 16-30												
Vaccine Period May, 1-15	*0.2%*	*8*	*1*	*0*	*0.0%*	*0*	*0*	*0*	*0.0%*	*0*	*0*	*0*

Table S5: Demographic and clinical characteristics of the comparative groups for people aged 50-59. Values are presented for the study period - August 13, 2021, to October 10, 2021.

Group	Nonbooster group Person-days at risk = 12,735,098				Booster group (days 12+) Person-days at risk = 17,239,405				Early post-booster group (days 3-7) Person-days at risk = 2,675,722			
	% person days at risk	# positive infections	# severe COVID-19	# COVID-19 deaths	% person days at risk	# positive infections	# severe COVID-19	# COVID-19 deaths	% person days at risk	# positive infections	# severe COVID-19	# COVID-19 deaths
Female	52.8%	5,705	43	2	49.5%	475	2	0	50.5%	690	1	0
Male	47.2%	4,542	76	5	50.5%	536	3	1	49.5%	831	3	0
General Jewish	69.9%	7,870	77	5	87.3%	841	4	1	85.4%	1,328	4	0
Arab	26.0%	1,652	37	2	9.2%	94	0	0	11.2%	103	0	0
Ultra-Orthodox Jewish	4.1%	725	5	0	3.5%	76	1	0	3.4%	90	0	0
Vaccine Period Jan, 16-31	10.1%	1,466	24	2	28.4%	316	1	0	24.7%	448	3	0
Vaccine Period Feb, 1-15	26.3%	3,100	42	3	46.1%	440	2	1	42.8%	686	0	0
Vaccine Period Feb, 16-28	18.9%	1,945	12	0	15.4%	171	0	0	16.5%	222	0	0
Vaccine Period Mar, 1-15	18.5%	1,722	20	1	7.0%	53	2	0	9.2%	100	1	0
Vaccine Period Mar, 16-31	20.3%	1,662	16	1	2.9%	28	0	0	5.5%	55	0	0
Vaccine Period Apr, 1-15	4.7%	301	4	0	0.2%	2	0	0	1.0%	9	0	0
Vaccine Period Apr, 16-30	1.0%	45	1	0	0.0%	1	0	0	0.2%	1	0	0
Vaccine Period May, 1-15	0.2%	6	0	0	0.0%	0	0	0	0.0%	0	0	0

Table S6: Demographic and clinical characteristics of the comparative groups for people aged 40-49. Values are presented for the study period - August 20, 2021, to October 10, 2021.

Group	Nonbooster group Person-days at risk = 16,560,386				Booster group (days 12+) Person-days at risk = 14,362,014				Early post-booster group (days 3-7) Person-days at risk = 2,866,033			
	% person days at risk	# positive infections	# severe COVID-19	# COVID-19 deaths	% person days at risk	# positive infections	# severe COVID-19	# COVID-19 deaths	% person days at risk	# positive infections	# severe COVID-19	# COVID-19 deaths
Female	51.0%	9,320	20	0	49.5%	573	2	0	50.3%	908	2	0
Male	49.0%	7,565	29	2	50.5%	584	1	0	49.7%	886	1	0
General Jewish	71.4%	12,370	29	2	87.4%	952	3	0	85.4%	1,479	3	0
Arab	24.2%	3,159	16	0	8.6%	135	0	0	10.9%	156	0	0
Ultra-Orthodox Jewish	4.4%	1,356	4	0	3.9%	70	0	0	3.7%	159	0	0
Vaccine Period Jan, 16-31	6.5%	1,434	10	0	17.3%	223	1	0	14.6%	337	0	0
Vaccine Period Feb, 1-15	14.1%	2,837	6	2	30.9%	344	0	0	27.2%	500	1	0
Vaccine Period Feb, 16-28	23.9%	4,227	12	0	34.2%	407	2	0	32.8%	615	1	0
Vaccine Period Mar, 1-15	22.0%	3,632	14	0	12.3%	127	0	0	15.2%	222	1	0
Vaccine Period Mar, 16-31	26.0%	3,930	7	0	4.8%	54	0	0	8.4%	106	0	0
Vaccine Period Apr, 1-15	6.1%	719	0	0	0.4%	2	0	0	1.5%	11	0	0
Vaccine Period Apr, 16-30	1.3%	96	0	0	0.0%	0	0	0	0.3%	2	0	0
Vaccine Period May, 1-15	0.3%	10	0	0	0.0%	0	0	0	0.1%	1	0	0

Table S7: Demographic and clinical characteristics of the comparative groups for people aged 30-39. Values are presented for the study period - August 24, 2021, to October 10, 2021.

Group	Nonbooster group Person-days at risk = 19,338,294				Booster group (days 12+) Person-days at risk = 9,541,493				Early post-booster group (days 3-7) Person-days at risk = 2,470,306			
	% person days at risk	# positive infections	# severe COVID-19	# COVID-19 deaths	% person days at risk	# positive infections	# severe COVID-19	# COVID-19 deaths	% person days at risk	# positive infections	# severe COVID-19	# COVID-19 deaths
Female	49.9%	12,575	6	0	48.0%	479	0	0	49.2%	739	0	0
Male	50.1%	8,877	10	1	52.0%	363	1	0	50.8%	754	0	0
General Jewish	71.2%	14,785	8	1	86.2%	652	1	0	84.3%	1,127	0	0
Arab	22.8%	4,242	7	0	8.1%	111	0	0	10.8%	154	0	0
Ultra-Orthodox Jewish	6.0%	2,425	1	0	5.6%	79	0	0	5.0%	212	0	0
Vaccine Period Jan, 16-31	4.6%	1,197	2	1	12.3%	109	0	0	9.9%	206	0	0
Vaccine Period Feb, 1-15	7.9%	2,156	4	0	18.1%	162	0	0	15.2%	271	0	0
Vaccine Period Feb, 16-28	12.9%	3,195	1	0	26.3%	229	1	0	22.7%	391	0	0
Vaccine Period Mar, 1-15	29.0%	6,263	5	0	32.3%	239	0	0	33.3%	434	0	0
Vaccine Period Mar, 16-31	35.0%	7,099	3	0	10.1%	98	0	0	15.7%	171	0	0
Vaccine Period Apr, 1-15	8.3%	1,308	1	0	0.9%	4	0	0	2.7%	19	0	0
Vaccine Period Apr, 16-30	1.9%	214	0	0	0.1%	1	0	0	0.5%	1	0	0
Vaccine Period May, 1-15	0.4%	20	0	0	0.0%	0	0	0	0.1%	0	0	0

Table S8: Demographic and clinical characteristics of the comparative groups for people aged 16-29. Values are presented for the study period - August 29, 2021, to October 10, 2021.

Group	Nonbooster group Person-days at risk = 26,675,210				Booster group (days 12+) Person-days at risk = 9,727,114				Early post-booster group (days 3-7) Person-days at risk = 3,121,950			
	% person days at risk	# positive infections	# severe COVID-19	# COVID-19 deaths	% person days at risk	# positive infections	# severe COVID-19	# COVID-19 deaths	% person days at risk	# positive infections	# severe COVID-19	# COVID-19 deaths
Female	49.4%	12,771	6	0	48.0%	168	0	0	50.0%	772	0	0
Male	50.6%	9,670	4	0	52.0%	149	0	0	50.0%	839	0	0
General Jewish	61.6%	16,333	6	0	86.8%	254	0	0	82.9%	1,414	0	0
Arab	30.4%	3,869	2	0	7.5%	37	0	0	11.7%	99	0	0
Ultra-Orthodox Jewish	8.0%	2,239	2	0	5.8%	26	0	0	5.4%	98	0	0
Vaccine Period Jan, 16-31	2.6%	802	1	0	7.5%	27	0	0	6.0%	119	0	0
Vaccine Period Feb, 1-15	5.6%	1,682	1	0	14.6%	51	0	0	11.8%	245	0	0
Vaccine Period Feb, 16-28	13.6%	3,782	1	0	31.4%	97	0	0	26.1%	513	0	0
Vaccine Period Mar, 1-15	25.9%	6,415	2	0	32.5%	98	0	0	32.8%	497	0	0
Vaccine Period Mar, 16-31	37.3%	7,574	4	0	12.4%	37	0	0	18.8%	206	0	0
Vaccine Period Apr, 1-15	11.7%	1,872	1	0	1.4%	7	0	0	3.6%	30	0	0
Vaccine Period Apr, 16-30	2.6%	275	0	0	0.1%	0	0	0	0.8%	1	0	0
Vaccine Period May, 1-15	0.6%	39	0	0	0.0%	0	0	0	0.1%	0	0	0

Table S9. Estimated regression coefficients of the Poisson regression models for confirmed infection.

term	*Primary analysis*		*Secondary analysis*	
	estimate	*95% CI*	*estimate*	*95% CI*
(Intercept)	*-8.70*	*[-8.76, -8.64]*	*-9.18*	*[-9.32, -9.04]*
Age: 16-29	*Reference category*			
Age: 30-39	*0.21*	*[0.19, 0.23]*	*0.07*	*[0.00, 0.14]*
Age: 40-49	*0.08*	*[0.06, 0.10]*	*-0.01*	*[-0.08, 0.06]*
Age: 50-59	*-0.17*	*[-0.2, -0.15]*	*-0.16*	*[-0.23, -0.09]*
Age: 60-69	*-0.35*	*[-0.37, -0.32]*	*-0.31*	*[-0.38, -0.23]*
Age: 70-79	*-0.50*	*[-0.54, -0.47]*	*-0.48*	*[-0.56, -0.40]*
Age: 80+	*-0.50*	*[-0.55, -0.46]*	*-0.29*	*[-0.38, -0.20]*
Gender: female	*Reference category*			
Gender: male	*-0.18*	*[-0.19, -0.17]*	*0.09*	*[0.05, 0.12]*
Vaccine Period Jan, 16-31	*Reference category*			
Vaccine Period Feb, 1-15	*-0.08*	*[-0.11, -0.06]*	*-0.08*	*[-0.12, -0.03]*
Vaccine Period Feb, 16-28	*-0.18*	*[-0.21, -0.15]*	*-0.08*	*[-0.13, -0.02]*
Vaccine Period Mar, 1-15	*-0.26*	*[-0.29, -0.24]*	*-0.21*	*[-0.27, -0.15]*

Vaccine Period Mar, 16-31	*-0.33*	*[-0.35, -0.30]*	*-0.25*	*[-0.33, -0.17]*
Vaccine Period Apr, 1-15	*-0.46*	*[-0.5, -0.42]*	*-0.37*	*[-0.57, -0.16]*
Vaccine Period Apr, 16-30	*-0.61*	*[-0.69, -0.54]*	*-0.89*	*[-1.58, -0.19]*
Vaccine Period May, 1-15	*-0.85*	*[-1.06, -0.63]*	*-0.98*	*[-2.94, 0.98]*
Sector: Arab	*Reference category*			
Sector: General Jewish	*0.31*	*[0.29, 0.33]*	*0.14*	*[0.08, 0.21]*
Sector: Ultra-Orthodox Jewish	*0.70*	*[0.67, 0.73]*	*0.64*	*[0.56, 0.73]*
Incidence group: 0%-10% decile	*Reference category*			
Incidence group: 10%-20% decile	*0.73*	*[0.67, 0.80]*	*0.66*	*[0.52, 0.79]*
Incidence group: 20%-30% decile	*1.02*	*[0.96, 1.09]*	*1.02*	*[0.89, 1.15]*
Incidence group: 30%-40% decile	*1.26*	*[1.20, 1.32]*	*1.30*	*[1.18, 1.43]*
Incidence group: 40%-50% decile	*1.44*	*[1.38, 1.51]*	*1.47*	*[1.35, 1.59]*
Incidence group: 50%-60% decile	*1.64*	*[1.58, 1.7]*	*1.58*	*[1.46, 1.7]*
Incidence group: 60%-70% decile	*1.80*	*[1.74, 1.86]*	*1.71*	*[1.60, 1.83]*
Incidence group: 70%-80% decile	*1.95*	*[1.89, 2.01]*	*1.85*	*[1.74, 1.97]*
Incidence group: 80%-90% decile	*2.08*	*[2.02, 2.14]*	*1.93*	*[1.81, 2.05]*

Incidence group: 90%-100% decile	*2.36*	*[2.3, 2.42]*	*2.27*	*[2.15, 2.38]*
Age group & nonbooster cohort	*Reference category (for each age group)*			
Age: 60+ & booster cohort	*-2.51*	*[-2.55, -2.47]*	*-2.01*	*[-2.06, -1.95]*
Age: 50-59 & booster cohort	*-2.50*	*[-2.56, -2.43]*	*-1.98*	*[-2.06, -1.9]*
Age: 40-49 & booster cohort	*-2.28*	*[-2.34, -2.22]*	*-1.69*	*[-1.76, -1.62]*
Age: 30-39 & booster cohort	*-2.20*	*[-2.27, -2.13]*	*-1.58*	*[-1.67, -1.49]*
Age: 16-29 & booster cohort	*-2.84*	*[-2.96, -2.73]*	*-2.38*	*[-2.50, -2.26]*

Table S10. Estimated regression coefficients of the Poisson regression models for severe COVID-19.

term	Primary analysis		Secondary analysis	
	estimate	95% CI	estimate	95% CI
(Intercept)	-13.84	[-14.29, -13.39]	-15.56	[-17.02, -14.10]
Age: 40-49	Reference category			
Age: 50-59	1.07	[0.74, 1.39]	0.32	[-0.72, 1.36]
Age: 60-69	1.97	[1.66, 2.27]	2.26	[1.25, 3.26]
Age: 70-79	2.79	[2.48, 3.09]	3.10	[2.11, 4.09]
Age: 80+	3.74	[3.45, 4.04]	4.24	[3.26, 5.23]
Gender: female	Reference category			
Gender: male	0.66	[0.55, 0.77]	0.66	[0.43, 0.89]
Vaccine Period Jan, 16-31	Reference category			
Vaccine Period Feb, 1-15	-0.15	[-0.28, -0.02]	0.02	[-0.24, 0.27]
Vaccine Period Feb, 16-28	-0.32	[-0.53, -0.12]	0.29	[-0.2, 0.78]
Vaccine Period Mar, 1-15	-0.43	[-0.65, -0.22]	0.17	[-0.44, 0.79]
Vaccine Period Mar, 16-31	-0.69	[-0.94, -0.45]	0.16	[-0.74, 1.06]
Vaccine Period Apr, 1-15	-0.70	[-1.14, -0.25]	-13.81*	[-1541.99, 1514.37]
Vaccine Period Apr, 16-30	-0.56	[-1.55, 0.42]	-11.39*	[-1298.62, 1275.83]

Vaccine Period May, 1-15	*0.45*	*[-1.51, 2.42]*	*-9.96**	*[-3921.00, 3901.08]*
Sector: Arab	*Reference category*			
Sector: General Jewish	*-0.44*	*[-0.6, -0.28]*	*-0.13*	*[-0.61, 0.36]*
Sector: Ultra-Orthodox Jewish	*-0.11*	*[-0.39, 0.17]*	*0.01*	*[-0.69, 0.71]*
Incidence group: 0%-10% decile	*Reference category*			
Incidence group: 10%-20% decile	*0.45*	*[0.05, 0.85]*	*0.61*	*[-0.55, 1.77]*
Incidence group: 20%-30% decile	*0.80*	*[0.44, 1.16]*	*1.29*	*[0.23, 2.34]*
Incidence group: 30%-40% decile	*1.29*	*[0.94, 1.64]*	*1.34*	*[0.3, 2.38]*
Incidence group: 40%-50% decile	*1.26*	*[0.9, 1.63]*	*0.91*	*[-0.16, 1.97]*
Incidence group: 50%-60% decile	*1.18*	*[0.81, 1.55]*	*1.16*	*[0.12, 2.2]*
Incidence group: 60%-70% decile	*1.63*	*[1.27, 1.98]*	*1.66*	*[0.64, 2.67]*
Incidence group: 70%-80% decile	*1.64*	*[1.28, 1.99]*	*1.54*	*[0.51, 2.56]*
Incidence group: 80%-90% decile	*1.91*	*[1.56, 2.26]*	*1.41*	*[0.37, 2.44]*
Incidence group: 90%-100% decile	*1.97*	*[1.62, 2.32]*	*2.02*	*[1, 3.04]*
Age group & nonbooster cohort	*Reference category (for each age group)*			
Age: 60+ & booster cohort	*-2.88*	*[-3.05, -2.71]*	*-1.87*	*[-2.1, -1.64]*
Age: 40-59 & booster cohort	*-3.08*	*[-3.79, -2.37]*	*-1.30*	*[-2.32, -0.28]*

* Estimated coefficients on the boundary due to rare events

Table S11. Estimated regression coefficients of the Poisson regression models for death due to COVID-19.

term	*Primary analysis*		*Secondary analysis*	
	estimate	*95% CI*	*estimate*	*95% CI*
(Intercept)	*-13.30*	*[-14, -12.6]*	*-13.79*	*[-15.64, -11.94]*
Age: 60-69	*Reference category (for each age group)*			
Age: 70-79	*1.06*	*[0.71, 1.41]*	*1.29*	*[0.53, 2.04]*
Age: 80+	*2.44*	*[2.13, 2.76]*	*2.48*	*[1.77, 3.2]*
Gender: female	*Reference category (for each age group)*			
Gender: male	*0.86*	*[0.64, 1.09]*	*0.85*	*[0.38, 1.31]*
Vaccine Period Jan, 16-31	*Reference category (for each age group)*			
Vaccine Period Feb, 1-15	*-0.24*	*[-0.5, 0.02]*	*-0.48*	*[-1.05, 0.1]*
Vaccine Period Feb, 16-28	*-0.10*	*[-0.51, 0.32]*	*0.02*	*[-1.15, 1.2]*
Vaccine Period Mar, 1-15	*-0.28*	*[-0.73, 0.17]*	*0.04*	*[-1.38, 1.47]*
Vaccine Period Mar, 16-31	*-0.65*	*[-1.28, -0.02]*	*-15.04**	*[-2798.11, 2768.02]*
Vaccine Period Apr, 1-15	*0.16*	*[-1.25, 1.57]*	*-12.84**	*[-6065.6, 6039.92]*
Sector: Arab	*Reference category (for each age group)*			
Sector: General Jewish	*-0.67*	*[-1.06, -0.28]*	*-0.07*	*[-1.26, 1.12]*
Sector: Ultra-Orthodox Jewish	*-0.27*	*[-0.88, 0.35]*	*0.16*	*[-1.36, 1.68]*

Incidence group: 0%-10% decile	*Reference category (for each age group)*			
Incidence group: 10%-20% decile	*0.36*	*[-0.4, 1.12]*	*-16.72**	*[-3782.11, 3748.67]*
Incidence group: 20%-30% decile	*0.84*	*[0.17, 1.51]*	*0.58*	*[-1.06, 2.22]*
Incidence group: 30%-40% decile	*1.45*	*[0.81, 2.1]*	*0.80*	*[-0.72, 2.32]*
Incidence group: 40%-50% decile	*1.48*	*[0.81, 2.15]*	*0.35*	*[-1.22, 1.93]*
Incidence group: 50%-60% decile	*1.09*	*[0.38, 1.81]*	*-0.19*	*[-1.84, 1.46]*
Incidence group: 60%-70% decile	*1.71*	*[1.05, 2.37]*	*0.67*	*[-0.83, 2.16]*
Incidence group: 70%-80% decile	*1.71*	*[1.03, 2.38]*	*0.54*	*[-0.98, 2.06]*
Incidence group: 80%-90% decile	*1.92*	*[1.25, 2.59]*	*-0.30*	*[-1.97, 1.38]*
Incidence group: 90%-100% decile	*2.16*	*[1.5, 2.83]*	*1.19*	*[-0.31, 2.68]*
Nonbooster cohort	*Reference category (for each age group)*			
Booster cohort	*-2.68*	*[-3.06, -2.31]*	*-1.59*	*[-2.07, -1.12]*

* Estimated coefficients on the boundary due to rare events

Table S12. Summary of estimated rates of confirmed infection, severe illness and death in the older age groups, and rate differences between the booster and nonbooster group and between day 12+ post-booster vaccination and day 3-7 post-booster vaccination.
All numbers are reported as events per 100,000 person-days at risk.

Outcome	Age	Incidence rate in the nonbooster group	Incidence rate in the booster group days 12+	Incidence rate in the early post-booster group (days 3-7)	Adjusted rate difference between booster days 12+ and nonbooster	Adjusted rate difference between day booster days 12+ and booster days 3-7
Confirmed infection	60+	62.0	5.1	39.7	57.0	34.4
	50-59	75.2	6.2	44.4	69.0	38.3
	40-49	91.1	9.3	46.8	81.7	38.2
	30-39	100.6	11.1	46.5	89.5	36.9
	16-29	76.6	4.5	39.3	72.2	35.7
Severe Illness	60+	5.7	0.3	2.3	5.4	1.9
	40-59	0.6	0.03	0.12	0.6	0.1
Death	60+	2.3	0.2	1.0	2.1	0.8

Table S13. Summary of the Poisson regression analysis of confirmed infections comparing the booster and nonbooster groups, with breakdown for age groups above 60 years of age.
For each group, we provide the number of confirmed infections, the total number of person-days at risk, and the estimated rate ratio for the primary analysis (nonbooster relative to at least 12 days post booster-vaccination) and the secondary analysis (3-7 days post booster-vaccination relative to at least 12 days post booster-vaccination).

Age	Nonbooster group infections (person-days at risk)	Booster group (days 12+) infections (person-days at risk)	Early post-booster (days 3-7) group infections (person-days at risk)	Rate ratio nonbooster relative to booster days 12+ [95% CI]	Rate ratio booster days 3-7 relative to booster days 12+ (95% CI)
80+	1,924 (4,069,797)	653 (10,237,630)	406 (1,084,200)	8.7 [8.0, 9.6]	5.4 [4.8, 6.2]
70-79	3,495 (6,948,415)	915 (19,543,388)	781 (2,065,488)	13.3 [12.3, 14.3]	7.7 [7.0, 8.5]
60-69	7,037 (11,784,920)	1,265 (23,551,510)	1,274 (2,695,147)	13.4 [12.6, 14.2]	8.2 [7.6, 8.9]
50-59	10,247 (12,735,098)	1,011 (17,239,405)	1,521 (2,675,722)	12.2 [11.4, 13.0]	7.2 [6.7, 7.9]
40-49	16,885 (16,560,386)	1,157 (14,362,014)	1,794 (2,866,033)	9.7 [9.2, 10.4]	5.4 [5.0, 5.8]
30-39	21,452 (19,338,294)	842 (9,541,493)	1,493 (2,470,306)	9.0 [8.4, 9.7]	4.9 [4.5, 5.3]
16-29	22,441 (26,675,210)	317 (9,727,114)	1,611 (3,121,950)	17.2 [15.4, 19.2]	10.8 [9.6, 12.2]

Table S14. Summary of the Poisson regression analysis of severe COVID-19 cases comparing the booster and nonbooster groups, with breakdown for age groups above 60 years of age.
For each group, we provide the number of confirmed infections, the total number of person-days at risk, and the estimated rate ratio for the primary analysis (nonbooster relative to at least 12 days post booster-vaccination) and the secondary analysis (3-7 days post booster-vaccination relative to at least 12 days post booster-vaccination).

Age	Nonbooster group infections (person-days at risk)	Booster group (days 12+) infections (person-days at risk)	Early post-booster (days 3-7) group infections (person-days at risk)	Rate ratio nonbooster relative to booster days 12+ [95% CI]	Rate ratio booster days 3-7 relative to booster days 12+ (95% CI)
80+	432 (3,942,195)	88 (8,973,006)	61 (1,069,276)	14.7 [11.6, 18.5]	5.8 [4.2, 8]
70-79	312 (6,766,093)	46 (17,158,718)	48 (2,037,645)	23.4 [17.1, 32]	9.0 [6, 13.4]
60-69	233 (11,426,723)	32 (20,537,071)	20 (2,626,386)	17.3 [11.9, 25.1]	4.9 [2.8, 8.6]

Table S15. Summary of the results of the primary and secondary analyses along with the results of the sensitivity analysis using a matching-based approach.

Outcome	Age	Rate ratio nonbooster relative to booster days 12+ [95% CI]	Rate ratio booster days 3-7 relative to booster days 12+ (95% CI)	Rate ratio nonbooster relative to booster day 12+ in the matching analysis [95% CI]
Confirmed infection	60+	12.3 [11.8, 12.8]	7.4 [7.0, 7.8]	9.5 [7.8, 11.4]
	50-59	12.2 [11.4, 13]	7.3 [6.7, 7.9]	9.4 [5.2, 13.0]
	40-49	9.7 [9.2, 10.3]	5.4 [5.0, 5.8]	8.4 [6.2, 10.6]
	30-39	9 [8.4, 9.7]	4.8 [4.4, 5.2]	7.3 [5.7, 8.7]
	16-29	17.2 [15.4, 19.2]	11.2 [9.9, 12.8]	13.3 [5.9, 18.8]
Severe illness	60+	17.9 [15.1, 21.2]	6.5 [5.1, 8.2]	12.4 [4.3, 30.4]